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10/680,316	10/08/2003	James L. Hartley	0942.285000M	3915

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER
SCHLAPKOHL, WALTER

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/680,316	**Applicant(s)** HARTLEY ET AL.	
	Examiner Walter Schlapkohl	**Art Unit** 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-59 and 61-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-59 and 61-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 5/5/2006 and 6/23/2006 in which claims 52 and 55-59 were amended. Claims 52-59 and 61-67 are pending and under examination in the instant Office action.

Information Disclosure Statement

The information disclosure statement filed 6/23/2006 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of French patent FR2 670 502 (IDS Ref. A120) that is not in the English language and is listed on the sixth supplemental IDS. It has been placed in the application file, but the information referred to therein has not been considered.

The information disclosure statement filed 6/23/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specifically, no copy of the unpublished U.S. Patent Application No. 10/633,690, listed in the fifth supplemental IDS, was provided.

Specification

The disclosure is objected to because of the following informalities: the first line of the specification does not reflect the updated status of the applications from which priority is claimed. For example, Application 09/907,900 is now abandoned and Application 09/498,074 is now U.S. Patent No. 6,720,140.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Applicant's amendment of claims 55-59 is found remedial and the rejection of claims 55-59 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby WITHDRAWN.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 52-59, 61 and 67 are rejected under 35 U.S.C. 102(e) as being anticipated by Griffiths et al (US Patent No. 6,010,884; IDS Ref. No. AK3) as evidenced by vector maps obtained from the New England Biolabs and Fermentas websites. **This is a new rejection not necessitated by Applicant's amendment.**

Note: Examiner has interpreted "recombination site" to include restriction enzyme sites since the term "recombination site" has not been defined in the specification.

Griffiths et al teach a method of cloning comprising (a) amplifying a nucleic acid template (NQ11) with a first primer comprising at least a first recombination site and a second primer comprising at least a second recombination site, wherein said first and second recombination sites do not recombine with each other; and (b) combining *in vitro* an amplified DNA product nucleic acid molecule flanked by a first recombination site and a second recombination site, wherein the recombination sites do not recombine with each other, with at least one first vector comprising a third and fourth recombination sites that do not recombine with each other, under conditions such that recombination occurs between said first and third and said second and fourth recombination sites, thereby producing a product vector (see entire document, especially column 16, lines 33-60). Regarding claim 53, Griffiths et al teach such a method wherein the amplification is accomplished by an amplification reaction (see, e.g., column 16, lines 50-53). Regarding claim 54, Griffiths et al teach such a method further comprising inserting said product vector into a host cell (see, e.g., column 16, lines 53-60). Regarding claims 55, Griffiths et al teach such a method wherein said first vector is an expression vector (see, e.g., column 16, lines 35-39). Regarding claims 56-59, Griffiths et al teach such a method wherein the vector comprises a promoter (P_{lac}), an origin or replication (ColE1) and a selectable marker (ampicillin resistance). Regarding claim 67, Griffiths et al teach such a method wherein said product nucleic acid molecule and said vector are combined in the presence of at least one recombination protein inherent in the ligation mixture (see, e.g., column 16, lines 53-57).

Response to Arguments

Applicant's arguments regarding the rejection of claims 52-59 and 61-67 under 35 U.S.C. 102(e) as being anticipated by Griffiths et al (US Patent No. 5,962,255) have been carefully considered and found persuasive. The recited rejection is hereby WITHDRAWN.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

This is a new rejection not necessitated by Applicant's amendment.

Claims 52-59 and 61-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al (WO 96/40724; Second Supplemental IDS Ref. No. AP7) in view of Shuman (US Patent No. 5,766,891; IDS Ref. No. AH2).

Hartley et al teach a method for cloning or subcloning an amplified nucleic acid molecule comprising: combining *in vivo* or *in vitro* (i) an "Insert Donor" DNA molecule comprising a desired DNA segment flanked by a first recombination site and a second recombination site, wherein the first and second recombination sites do not recombine with each other; and (ii) a "Vector Donor" DNA molecule containing a third recombination site and a fourth recombination site, wherein the third and fourth recombination sites do not recombine with each other under conditions such that recombination occurs between said first and third and said second and fourth recombination sites, thereby producing a product vector (see, e.g., page 7, lines 7-21). Hartley et al further teach that the insert can be a PCR product with e.g. "an attB site at one end and a loxP site at the other end" (see, e.g., page 18, lines 14-25; and page 30, lines 24-27). Thus, Hartley et al teach a method for cloning or subcloning an amplified nucleic acid molecule comprising (a) using an amplified a nucleic acid product such that the nucleic acid comprises a first and second recombination site, wherein said first and second recombination sites do not recombine with each other and (b) combining *in vitro* the amplified DNA product nucleic acid molecule flanked by a first recombination site and a second recombination site wherein the recombination sites do not recombine with each other with at least one first vector comprising a third and fourth recombination sites that do not recombine with each other, under conditions such that recombination occurs between said first and third and said second and fourth recombination sites, thereby producing a product vector (see entire document, especially page 7, lines 5-19; page 18, lines 24-25; page 21, lines 24-29; and page 30, lines 20-28). Hartley et al further teach that such a method possesses several advantages including free adjustment of *in vitro* reaction conditions to optimize enzyme activities and the ability to use DNA molecules that would otherwise be incompatible with a desired biological host (see, e.g., page 8, lines 21-29). Regarding claim 54, Hartley et al teach such a method further comprising inserting said product vector into a host cell (see, e.g., page 13, lines 4-8; page 15, lines 8-13; and page 17, lines 17-20). Regarding claims 55-59, Hartley et al teach such a method wherein the first vector is an expression vector comprising a selectable marker, and an origin of replication (see, e.g., page 18, lines 17-31; page 18, lines 1-2 and Figures 35 and 39). Regarding claims 62-66, Hartley et al teach such a method wherein said first, second, third or fourth recombination sites are loxP and loxP511 sites, and attB, attP, attL and attR sites (e.g., page 19, lines 25-29 and page 23, lines 13-25). Regarding claim 67, Hartley et al teach such a method wherein the nucleic acid molecule and the first vector are combined in the presence of at least one recombination protein (see, e.g., page 7, lines 15-17).

Hartley et al do not disclose methods of PCR amplification to synthesize the double-stranded DNA with the recombination sites at each end, wherein the primers comprise the recombination sites.

Shuman discloses methods of synthesizing double-stranded DNA molecules by PCR amplification. The resultant molecule comprises the primer sequence at each 5′ and 3′ end (see, e.g., column 6, lines 46-56). Shuman uses topoisomerase recognition sites for primer sequences (see, e.g., column 21, claim 1).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to amplify the insert to be used in recombination by Hartley et al with the method of PCR taught by Shuman et al because Hartley et al teach that it is within the ordinary skill of the art to use double-stranded PCR products with recombination sites at either end for recombinational cloning and because Shuman teaches that it is within the ordinary skill of the art to generate double-stranded molecules for cloning using PCR primers comprising the recombination sites.

One of ordinary skill in the art would have been motivated to combine the methods of Hartley et al with those of Shuman et al for the expected benefit of generating the PCR products with first and second recombination sites at either end, which sites that Hartley et al teach as required for their more advantageous method of cloning, the advantages including free adjustment of *in vitro* reaction conditions to optimize enzyme activities and the ability to use DNA molecules that would otherwise be incompatible with a desired biological host.

Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when combining the method of PCR amplification as taught by Shuman in the method of cloning as taught by Hartley et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-59 and 61-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 10/815,730. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated by, or would have been obvious over, the reference claims.

This rejection is maintained for reasons of record recited in the previous Office Action.

Conclusion

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative.

NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Thursday from 8:30 AM to 6:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

July 15, 2006

NANCY VOGEL
PRIMARY EXAMINER